REMARKS

The invention resides in the surprising discovery that adenosine preferentially binds the platelet membrane receptor protein gpIIb/IIIa and thus is able to inhibit the activation of this protein. The ability of adenosine to prevent this activation results in an ability to inhibit platelet aggregation or thrombosis where these conditions are undesired and are mediated by activation of this gpIIb/IIIa protein. None of the art cited by the Office describes or suggests this property of adenosine.

Proposed new claims 21-33 focus on this surprising discovery. Support for these claims is found in Example 5, on pages 11-12, which demonstrates the ability of adenosine to bind gpIIb/IIIa and by Example 6, on page 12, that demonstrates adenosine's resulting ability to inhibit platelet aggregation. The claims are further supported by Example 8, which demonstrates the ability of adenosine to inhibit the binding of fibrinogen to gpII/IIIa. Thus no new matter is added by the proposed claims.

Applicants greatly appreciate the rejoinder of claims 3-4 and 12-13 with the elected claims of group I. The proposed new claims encompass the subject matter of these elected claims, and are proposed for greater clarity with respect to the nature of the invention. The kind consideration shown by the Examiner in rejoining the subject matter of groups I and II is sincerely appreciated.

Formal Drawings are enclosed.

The Rejection Under 35 U.S.C. § 112, Paragraph 2

It is believed that the claims are presently proposed address the rejections made under this section of the statute. The definition of "effective amount" is now set forth clearly in the claims - it is an amount "effective in inhibiting the activation of platelet membrane receptor protein gpIIb/IIIa. The language "according to" has been replaced by "of." "LMW" has been

spelled out. Where claims are multiply dependent, the dependence is expressed in the alternative.

Should there be further concerns regarding wording of the claims, a telephone call to the undersigned is respectfully requested. It may be possible to work out alternative wording by Examiner's amendment or by phone.

The Rejection Under 35 U.S.C. § 102

Claims 1-6, 10-15 and 19-20 were rejected as assertedly anticipated by Sollevi (U.S. 5,731,296). These claims were directed to inhibiting platelet aggregation inhibiting thrombosis and to treating thromboembolytic disorders in a mammal, including specific conditions and including additional treatment with an antithrombotic.

The claims as amended address this rejection by adding the additional limitation that the disorders to be treated must be associated with a malfunction of the gpIIb/IIIa protein receptor. Not all conditions which are characterized by platelet aggregation or thrombosis are associated with gpIIb/IIIa. Other mechanisms for such conditions exist; the claims are directed only to those conditions associated with inappropriate activity of the gpIIb/IIIa receptor. The Sollevi document is silent with respect to this limitation.

Further, the cited portions of Sollevi do not appear to describe adenosine as being administered for treating arterial thrombosis or ischemia although Sollevi does indicate that adenosine may inhibit clot formation under certain conditions (column 3, lines 12-15) and may inhibit platelet aggregation (column 20, lines 20-23). However, there is no indication in Sollevi that such inhibition is due to the effect of adenosine on the receptor protein gpIIb/IIIa.

The thrust of the Sollevi disclosure is that adenosine is useful as a vasodilator. This is a completely different effect from inhibition based on binding to gpIIb/IIIa as required by the claims. The apparent purpose of the infusion of adenosine according to Sollevi is, rather,

vasodilation of the arteries without dilation of the veins. This is unrelated to the activity claimed herein.

Claims 2, 5 and 6 were rejected as assertedly anticipated by Wang, *et al.*, an abstract which describes inhibition of thrombus formation in stenosed canine coronary arteries by adenosine. Adenosine was used in combination with aspirin, one of the other antithrombotics set forth in claim 6 and present in proposed claims 25, 30 and 33.

Again, Wang does not anticipate because Wang fails to describe or suggest the claim limitation that adenosine inhibits the activity of gpIIb/IIIa. Wang does not inherently anticipate because the animal model does not display a platelet membrane receptor protein gpIIb/IIIa associated disorder. Rather, the thrombosis was produced by mechanical perturbation.

Because neither of the above documents describes each and every limitation of the claims, neither document anticipates the claims as presently proposed.

The Rejection Under 35 U.S.C. § 103

The rejection was applied to claims 16-18 which were directed to kits for constructing a pharmaceutical composition. This would correspond to new claims 31-33. The rejection was made over a combination of Sollevi as set forth above in combination with Foster (U.S. 4,444,879). Foster is cited to show that providing components of a kit is known in the art.

Claims 31-33, however, are not rendered obvious by this combination for the same reason that claims 21-30 are not anticipated by Sollevi. There is nothing in Sollevi that suggests a pharmaceutical composition, a method or a kit designed to treat or prevent platelet membrane receptor protein gpIIb/IIIa associated disorders. Thus, there is no incentive to construct a kit for this purpose and claims 31-33 are not rendered obvious by this combination.

Additional Art

Four additional documents were cited but not applied as part of a rejection. None of these documents suggests the claim limitation that adenosine be used to treat disorders associated with the membrane receptor glycoprotein gpIIb/IIIa. The Kutsuna document, characterized by the Office as reporting adenosine to have this property does not, in fact, appear to contain this disclosure. On the contrary, adenosine is reported there to inhibit platelet aggregation induced by adenosine diphosphate; there is no suggestion of inhibiting the gpIIb/IIIa receptor.

The remaining documents do not disclose this property either.

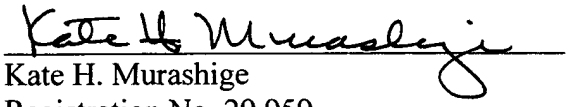
CONCLUSION

As the proposed claims contain the limitation of affecting the receptor protein gpIIb/IIIa specifically, and as none of the cited documents disclose this property, it is believed that the proposed new claims 21-33 are in a position for allowance and passage of these claims to issue is respectfully requested. If minor wording matters remain that can be addressed by telephone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 205032000420.

Respectfully submitted,

Dated: April 16, 2003

By: 

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